Approaches to Assess the Health Effects of Bioactive Food Component: Cardiovascular Disease

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Assessing the Health Effects for What?

- **Health Claims for Food Labeling**

  Causal *relationship* between a nutrient or food and a disease (e.g., risk reduction) – effective dose may or may not be identified depending on whether it is a health claim (required) or qualified health claim* (depending on the available evidence) and if there is a Daily Value.

  ***Qualified health claims require less scientific evidence than health claims**

- **Dietary Reference Intakes (DRI)**

  Recommended intake levels (e.g., RDA) and tolerable upper intake levels

  Identify an *intake level* to achieve a health benefit (e.g., disease risk reduction)

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Application of Animal Data

- Useful in understanding the mechanism by which the bioactive food component has a beneficial role in human health
- Useful in identifying potential surrogate endpoints
- Useful in the safety evaluation of bioactive food components and for setting a tolerable upper intake level (DRI)
- *Not* useful in setting recommended intake levels or reviewing the evidence for a health claim

Essentiality of Surrogate Endpoints

Evidence that is considered useful for setting a DRI or allowing a health claim includes human intervention studies that measure:

Validated Surrogate Endpoints

CHD – LDL and total cholesterol, blood pressure

Incidence of the Disease

Myocardial infarction, ischemia, atherosclerosis, cardiovascular/sudden death

Surrogate endpoints may not be essential, but would eliminate conducting very long and expensive intervention studies on incidence

Essentiality of Surrogate Endpoints

- Very helpful in the evaluation of the relationship between a nutrient (bioactive food component) and a disease (CHD) (Health Claim).

- Very helpful in setting recommended intake levels - Estimated Average Requirement (EAR)* which is required to set a Recommended Dietary Allowance (RDA) – Difficult to establish an EAR based on "incidence" data

*EAR is the average daily intake level estimated to meet the requirement (provide a health benefit) for 50% of individuals in a particular life stage and gender group.

Case: Omega 3 DHA/EPA and CHD

- NO DRI set for EPA or DHA
- There was credible evidence for a qualified health claim*, but not for a health claim

*Qualified health claims require less credible evidence than health claims, therefore requiring qualifying language

Evidence for EPA and DHA

While most intervention studies on incidence showed a benefit,

- **Conducted in diseased populations (e.g., prior coronary event)**
- **Endpoints measured were not validated surrogate endpoints**
- **Involved fish, rather than EPA/DHA**

Evidence for EPA and DHA (cont.)

Surrogate endpoints for CHD,

- **One surrogate endpoint for EPA/DHA – blood pressure**
- **EPA/DHA not effective on blood pressure in healthy individuals, average dose to see a benefit in individuals with hypertension and hypercholesterolemia > 4g/day**
- **Studies conducted on other endpoints, not useful (e.g, LDL, restinosis, plaque stability)**
- **Included other nutrients besides EPA/DHA (*n*-6 fatty acids)**

Evidence for EPA/DAH

- **Strongest evidence for EPA/DHA and CHD for the general population is from observational studies**

- **EPA and DHA or some other component in fish?**

  Insufficient for an EAR/RDA or health claim on nutrient

  Sufficient for an Adequate Intake* or qualified health claim*

  ***Requires less scientific evidence than an RDA or health claim**

For future studies to be relevant for DRIs and Health Claims

- Identify animal models for evaluating safety and for identifying potential surrogate endpoints for a specific bioactive food component.
- Validate these potential surrogate endpoints in healthy humans.
- Conduct controlled human intervention studies in which the subjects are healthy or at high risk (e.g., hypercholesterolemic) and the specific bioactive food component is evaluated at multiple doses.
- If surrogate endpoints are not available, then will need to conduct intervention studies that measure disease incidence in healthy or high risk populations.

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